REMARKS

Reconsideration of the allowability of the present application in view of the above amendments and the following remarks is requested respectfully.

Status of the Claims

Claims 1 and 14 have been amended. Claims 4 to 6, previously withdrawn by the Examiner, have been cancelled without prejudice. Claims 15 to 20 have been cancelled without prejudice and the subject matter therein reinstated in newly added Claims 22 to 30. Claim 21 has been added and includes recitations carved out of amended Claim 14. Claims 31 to 33 have been added to define additional embodiments of the invention. Claim 3 was withdrawn erroneously by the Examiner and applicant requests its rejoinder with the elected claims. The claims presently pending are Claims 1 to 3, 7 to 14, and 21 to 33.

Discussion of the Amendments

Claim 1 has been amended to more particularly define the hirudin derivative. Support for this amendment is in the application at paragraph [0013].

Claim 14 has been amended to delete recitations relating to a step which is not essential to the claimed process. Dependent Claim 21 has been added to include recitations regarding this step.

Due to the requirement that dependent claims follow the claims from which they depend, Claims 15 to 20 have been cancelled without prejudice and the subject

matter therein reinstated in Claims 22 to 30. Claims 22 to 24 mirror cancelled Claims 15 to 17. Claim 23 includes changes from Claim 16 for clarification. Claim 25 reinstates the subject matter of Claim 18 except for recitations relating to a step which is not essential to the claimed process. These recitations are included in Claim 26. Claim 27 reinstates the subject matter of Claim 19 except for recitations relating to a step which is not essential to the claimed process. These recitations are included in Claim 28. Claim 29 reinstates the subject matter of Claim 20 except for recitations relating to a step which is not essential to the claimed process. These recitations are included in Claim 30. In addition, Claim 29 includes changes from Claim 20 to better clarify the process defined therein.

Claims 31 to 33 have been added to more particularly define applicant's invention. Support for these claims is in Examples 1 and 2 of the application.

The descriptive portion of the application have been amended to include the generic names for Leukine® and Refludan®.

Claims 4 to 6, previously withdrawn by the Examiner, have been cancelled without prejudice.

No new matter has been added.

Traversal of the Examiner's Rejection under Section 102(b)

The Examiner rejected Claims 1, 7 to 14, 18, and 19 under Section 102(b) as being anticipated by the disclosure of U.S. Patent No. 5,434,073 to Dawson et al.

The Examiner's rejection is traversed respectfully.

Each of these claims defines a nucleic acid which includes "Z" (see the formula in Claim 1). As defined in the claims, "Z" is a codon for arginine or lysine and is between "$S_x$", which encodes a signal or leader sequence, and "Hir", which encodes hirudin or a derivative thereof. Applicant's claims distinguish over the sequence disclosed by Dawson et al. in the recitation of "Z", as explained below.

Dawson et al. disclose specifically only two nucleic acids which encode a hirudin-containing fusion protein in which the sequence encoding hirudin (the "Hir" sequence) appears in the 5' direction from the sequence encoding "protein(Y)". These sequences encode "Hirudin-IEGR-Hirudin" and "Hirudin-IEGR-Streptokinin". In each of these sequences "$S_x$" corresponds to the sequence encoding the α-factor pre-pro-peptide which serves as a secretion signal sequence. "Hir" corresponds to the first hirudin-encoding sequence.

The Examiner claims that "Z" corresponds to the arginine (Arg) codon contained in a "linker sequence" encoding Ser-Leu-Asp-Lys-Arg. The Examiner's characterization of this sequence is incorrect, however. The Ser-Leu-Asp-Lys-Arg encoding sequence is not a "linker sequence". A close reading of Dawson et al. shows that, in the construction of the final nucleic acid, the 3' end of the α-factor pre-pro-peptide encoding sequence (which corresponds to $S_x$) is spliced off by a restriction enxyme. To rebuild this missing section of the sequence, the Ser-Leu-Asp-Lys-Arg encoding sequence is added on, thus reconstituting the α-factor pre-pro-peptide encoding sequence (which corresponds to $S_x$). As such, the arginine codon is actually part of the sequence corresponding to $S_x$ and not separate from it.

Given the above, none of the sequences of Dawson et al. contains a codon corresponding to "Z", as set forth in applicant's claims. Dawson et al., therefore, does not anticipate applicant's claims.

Traversal of the Examiner's Rejection under Section 103(a)

The Examiner rejected Claims 15 and 16 as being rendered obvious by Dawson et al. in view of U.S. Patent No. 5,095,092 to Badziong and Claim 17 as being rendered obvious by Dawson et al. in view of Bischoff et al., *J. Chromatography*, 476: 245-255 (1989).

The Examiner's rejections are traversed respectfully.

In both of the above cases, the Examiner relies on Dawson et al. as disclosing the production of a fusion protein using the nucleic acid of applicant's invention. As discussed above, however, Dawson et al. does not disclose the use of a nucleic acid of applicant's invention. None of the other references contain such disclosure. As suchy, the disclosures of the combined references do not teach or suggest the subject matter of applicant's claims. Accordingly, it is requested respectfully that the Section 103 rejections be withdrawn.

Discussion of the Examiner's Rejection Under the
Written Description Requirement of Section 112, First Paragraph

The Examiner has rejected Claims 1, 2, and 7 to 20 under the written description requirement of Section 112, first paragraph.

The Examiner's rejections are traversed respectfully.

MPEP § 2163 states that "[t]o satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention." The MPEP goes on to state that "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was 'ready for patenting' such as [] by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention."

The involved claims relate to a nucleic acid encoding a hirudin (or derivative thereof) - containing fusion protein and a method for using such a nucleic acid. Descriptions of the actual reduction to practice with respect to the nucleic acid are contained in the Examples section. Methods for using the same are also described.

In addition, identfying characteristics of the nucleic acid are described. As the Examiner is aware, the inventive aspect of the present invention resides in the discovery that a fusion protein containing hirudin (or a derivative thereof) may be exported from yeast with good yields. Accordingly, an identifying characteristic of the present invention is that the subject nucleic acid contains a sequence encoding hirudin or a derivative thereof and another protein. This identifying characteristic is well described throughout the application at paragraphs [0004] to [0014] and [0031] and in the Examples.

Given the above, there exists adequate description of an actual reduction to practice and of identifying characteristics respecting the subject nucleic acid to show to one skilled in the art that applicant was in possession of the claimed invention.

Discussion of the Examiner's Rejection Under the
Enablement Requirement of Section 112, First Paragraph

The Examiner has rejected Claims 1, 2, and 7 to 20 under the enablement requirement of Section 112, first paragraph. According to the Examiner, applicant has not enabled one skilled in the art to practice over the full scope of the claims without undue experimentation.

The Examiner's rejection is traversed respectfully.

The Examiner's attention is directed to MPEP § 2164.01(b) which states that "[a]s long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied. The MPEP goes on to state that "[f]ailure to disclose other methods by which the claimed invention may be made does not render a claim invalid under 35 U.S.C. 112."

As recognized by the Examiner, applicant has enabled examples of nucleic acids of the present invention and the relevant methods for using the same. As such, applicant has disclosed at least one method by which a nucleic acid of applicant's claims may be made (e.g., it may be made using the promoter, the leader sequence, the linker sequence, the sequence encoding "protein(Y)", and the expression-enhancing sequence used in the Examples) and at least one method by which the nucleic acid may

be used in the production of protein. Applicant need not enable every single method for making and using the nucleic acid using every possible promoter sequence, signal/leader sequence, linker sequence, sequence encoding "protein(Y)", or expression-enhancing sequence. By virtue of the fact that applicant has enabled at least one method for making the claimed nucleic acid and at least one method for using the claimed nucleic acid to make protein, one skilled in the art will know how to make and use the invention.

Discussion of the Examiner's Rejections Under Section 112, Second Paragraph

The Examiner has rejected Claim 17 under Section 112, second paragraph, because he considered the phrase "removing the protein encoded by protein(Y)" to be vague. It is submitted that this rejection has been overcome with the presentation of added Claim 24 which mirrors now cancelled Claim 17. The protein encoded by protein(Y) is released from the fusion protein. This may be done, for example, by cleaving the fusion protein with trypsin. For clarification, the phrase has been changed to "releasing the protein encoded by protein(Y) from the fusion protein". Similar language appears in Claim 20 and the Examiner has not objected to this language.

The Examiner has rejected Claim 1, 2, and 7 to 20 under Section 112, second paragraph, because the Examiner considers Claim 1 (from which the remaining claims depend) to be unclear as to what a "hirudin derivative" encompasses. This rejection has been overcome by the present amendment to Claim 1 in which "hirudin derivative" is defined as being a protein which is at least 40% homologous to a natural hirudin isoform.

Discussion of the Provisional Obviousness-type Double Patenting Rejections

The Examiner provisionally rejected Claim 1 under the doctrine of obviousness-type double patenting as being unpatentable over Claim 4 of U.S. Application No. 10/076,634. The Examiner also provisionally rejected Claim 1 under this doctrine as being unpatentable over Claim 2 of U.S. Application No. 10/076,631.

The Examiner's rejections at present are merely provisional as no patent upon which an obviousness-type double patenting rejection may be based has yet issued. Accordingly, it is submitted that no response is required at the present time.

Discussion of the Examiner's Objections
to the Descriptive Portion of the Specification

The Examiner objected to the descriptive portion of the specification because he noted various trademarks had been used throughout the application and requested that they be capitalized and accompanied by generic terminology.

Applicant notes that all trademarks are indeed capitalized. Applicants have amended the descriptive portion to include the generic names for Leukine® and Refludan®. The remaining trademarks, however, are company names and there are no generic names therefor.

Discussion of Claim 3

In his May 20, 2004 Action, the Examiner withdrew Claim 3 from further consideration as being directed to a non-elected invention. It is submitted respectfully that withdrawal is in error.

In his February 24, 2004 Requirement for Restriction, the Examiner grouped the claims into two claim groups: (I) Claims 1 to 3 and 7 to 20, drawn to a nucleic acid; a multicopy vector, a plasmid, and a host cell comprising the same; and a process using the same; and (II) Claims 4 to 6, drawn to a fusion protein. Applicant elected Group I, which included Claim 3, for further prosecution.

Although the Examiner further required an election of species and applicant's provisionally elected the species in which protein(Y) encodes mini-proinsulin or a derivative thereof (not covered by Claim 3), the claims were only to be restricted to this elected species if claims generic to elected and non-elected species were not found finally allowable. As such, Claim 3 was not to be withdrawn until the final Action in which the Examiner finally rejected Claim 1 (which is generic to the species).

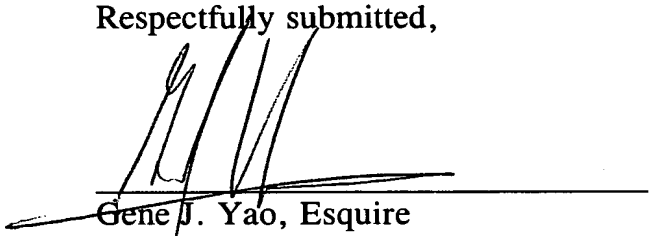
As the present Reply is being filed with a Request for Continued Examination, thus effectively withdrawing the finality of the previous rejection, applicant requests respectfully that the withdrawal of Claim 3 be rescinded.

Conclusion

In view of the above amendment and remarks, it is believed that the Examiner's rejections have been overcome.

An early and favorable reconsideration of the rejections and an early and favorable allowance of all of the pending claims are requested respectfully.

Respectfully submitted,



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